REMARKS

Claim 1-6, 8, 10-12, 14-18, 20, 22-24, 26-29, 31-37 are pending in this application. Claims 1, 12, 26, and 31 have been amended. New claims 35-37 have been added. Support for the amendments and the new claims is found in the specification and claims as filed and is discussed below. Applicants thank Examiner Isis Ghali for the courteous and helpful interview conducted with Applicants' representatives Rose M. Thiessen and Gregory A. Hermanson and on January 9, 2007. In response to the Office Action, and in accordance with the recent interview, Applicants submit the foregoing amendments and provides remarks addressing the claim rejections indicated in the Office Action.

Interview

Applicants thank Examiner Isis Ghali for the informative interview on January 9, 2007. The foregoing claim amendments and following remarks are submitted in light of the interview discussion and further analysis of the cited art.

New Claims

New claims 35-37 are added by the foregoing amendments. No new matter is added by these amendments. Support for the amended claims and the new claims is found in the specification and claims as filed.

Rejection of Claims 1-5, 8, 10-12, 14-17, 20, 23, 24, 26-29, and 31-34 Under 35 U.S.C. § 103(a)

Claims 1-5, 8, 10-12, 14-17, 20, 23, 24, 26-29, and 31-34 have been rejected under 35 U.S.C. § 103(a) as unpatentable over WO 96/10,374 (hereinafter "WO '374") in view of U.S. Patent number 6,143,352 ('352). Applicants traverse this rejection. To articulate a *prima facie* case of obviousness under 35 U.S.C. § 103(a), the PTO must, *inter alia*, cite prior art that teaches or suggests all the claimed limitations. *In re Royka*, 490 F.3d 982 (C.C.P.A. 1974); MPEP §2143.03.

As discussed in the interview on January 9, 2007 and as summarized in the remarks below, the cited references do not, either singly or in combination, teach or disclose all the elements of amended claims 1 and 12, shown below:

1. A stable liquid adhesive for sealing a wound, the adhesive comprising:
a cyanoacrylate;
a therapeutic agent comprising an antibiotic;
a defect forming agent capable of being removed from a cured cyanoacrylate matrix by solvation in an aqueous solution whereby a plurality of defects in the matrix are formed permitting release of the therapeutic agent from the matrix at a controlled rate; and
a protective shell surrounding the therapeutic agent that prevents premature polymerization of the adhesive by blocking direct contact between the therapeutic agent and the cyanoacrylate surrounding said therapeutic agent.

12. A method of sealing a wound, the method comprising the steps of:
approximating the wound;
applying a liquid adhesive to a tissue surface surrounding the wound, the liquid adhesive comprising a mixture of a cyanoacrylate, a therapeutic agent comprising an antibiotic, a protective shell surrounding the therapeutic agent preventing premature polymerization of the adhesive by blocking direct contact between the therapeutic agent and the cyanoacrylate surrounding said therapeutic agent, and a water soluble defect forming agent;
curing the adhesive, whereby the wound is sealed;
removing the defect forming agent from the cured adhesive by solvating the defect forming agent in a body fluid, whereby a plurality of defects in the cured adhesive are formed; and
delivering the antibiotic to the wound through the defects in the cured adhesive at a controlled rate, wherein the shell provides long-term controlled release of the antibiotic from the cured adhesive.

In the foregoing amendments, claims 1 and 12 were amended to clarify that the liquid adhesive includes *"a protective shell surrounding the therapeutic agent that prevents premature polymerization of the adhesive by blocking direct contact between the therapeutic agent and the cyanoacrylate surrounding said therapeutic agent."* Specifically, Applicant respectfully asserts neither WO '374 or the '352 patent disclose or teach such a limitation.

WO '374 teaches an adhesive composition comprising cyanoacrylate, PEG (a pore forming agent), and an active substance (e.g., an antibiotic). The '352 patent teaches a "biocompatible monomer composition, comprising an effective amount of at least one biocompatible pH modifier effective to regulate the pH of an immediate in vivo environment of the polymer to a pH range at which the polymer's in vivo biodegradation proceeds at a different

rate than it does at physiologic pH" ('352 col. 3, 1-10), and further teaches the pH modifier can be encapsulated so that (1) it is released from the microcapsule over a period of time during the biodegradation of the in situ polymer ('352, col. 7, 47-49), (2) to prevent pre-application effects of the pH modifier, thereby increasing shelf-life, and (3) facilitating handling of the monomer composition during use ('352, col. 7, 60-65). However, neither reference discloses that premature polymerization is a problem, much less teaches a novel solution to the problem.

As noted in the Office Action, the reference WO '374 "does not teach encapsulating the active substance." Although the '352 patent discloses a encapsulating for time release (e.g., encapsulating a pH modifier which can be a bioactive agent; '352, col. 10, 42-44), there is no disclosure of "a *protective shell preventing premature polymerization of the adhesive by blocking direct contact between the therapeutic agent and the cyanoacrylate surrounding said therapeutic agent*" as claimed in claims 1 and 12. The '352 patent does not recognize or mention premature polymerization. The '352 patent cannot teach what it does not disclose or suggest. Further, although the '352 patent discloses an encapsulation process that may provide some protection, there is no disclosure of forming a protective shell, nor it is not known whether or not such a process results in forming a protective shell that will prevent premature polymerization as portions of the drug may not be encapsulated, instead residing on the surface of the formed particles, or only partially encapsulated in the micro-fine particle.

Applicants discovered that cyanoacrylate adhesive mixtures having a microcapsule that substantially prevents direct contact of the antibiotic and the cyanoacrylate blocks undesired chemical interactions and avoids premature curing (polymerization and solidification) of the cyanoacrylate. Encapsulation also facilitates controlled release of the antibiotic from the cured cyanoacrylate adhesive through defects in the cured adhesive provided by solvation of the defect forming agent. The cited references, alone or in combination, do not teach or suggest such features of the cyanoacrylate adhesives as claimed.

In addition, to establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art

reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Applicant respectfully suggests that a *prima facie* case of obviousness has not been established. Here, as discussed above, neither the '352 patent or WO '374 teaches or suggests the limitation "*a protective shell surrounding the therapeutic agent that prevents premature polymerization of the adhesive by blocking direct contact between the therapeutic agent and the cyanoacrylate surrounding said therapeutic agent.*" In fact, neither reference discloses the problem of premature polymerization nor do they teach how to prevent premature polymerization. Further, Applicant respectfully suggest for at least the reason that neither reference even discloses problems associated with premature polymerization, there is no motivation in either the '352 patent or WO '374 to modify WO '374 with the teachings of the '352 patent to teach an adhesive that is formed to prevent premature polymerization.

Accordingly, Applicants respectfully request that this claim rejection be withdrawn for claims 1 and 12 and assert claims 1 and 12 are in condition for allowance, for at least the reasons discussed above. Because claims 2-5, 8, 10-11, 14-17, 20, 23, 24, 26-29, and 31-34 depend from claims 1 and 12 either directly or indirectly, Applicants also respectfully request that this claim rejection be withdrawn for claims 2-5, 8, 10-11, 14-17, 20, 23, 24, 26-29, and 31-34, and assert that these claims are also in condition for allowance for at least the same reasons.

Rejection of Claim 22 under 35 U.S.C. § 103(a)

Claim 22 has been rejected under 35 U.S.C. § 103(a) as unpatentable over WO 96/10,374 (hereinafter "WO '374") in view of U.S. Patent number 6,143,352 ('352) and in further in view of WO 96/00760 (WO '760). Applicants traverse these rejections for at least the reason that claim 22 depends directly from claim 12, which is asserted to be in condition for allowance as discussed above. After a careful review of the art, Applicants respectfully assert that the addition of WO '760 includes no additional disclosure overcoming the deficiencies of the WO '374 reference and the '352 patent in disclosing or teaching all the limitations of claims 1 and 12, nor does the Office Action state that it does. Instead, WO '760 merely discloses biomedical adhesives comprising a biocompatible pH modifier (*e.g.*, a microencapsulated pH modifier).

Accordingly, Applicants request that this rejection be withdrawn and respectfully assert claim 22 is in condition for allowance.

Rejection of Claims 6 and 18 under 35 U.S.C. § 103(a)

Claims 6 and 8 have been rejected under 35 U.S.C. § 103(a) as unpatentable over WO '374 in view of the '352 patent and further in view of WO 99/20685 (WO '685). Applicants traverse these rejections for at least the reason that claims 6 and 18 depend indirectly from claims 1 and 12, respectively, which are asserted to be in condition for allowance as discussed above. After a careful review of the art, Applicants respectfully assert that the addition of WO '685 includes no additional disclosure overcoming the deficiencies of the WO '374 reference and the '352 patent in disclosing or teaching all the limitations of claims 1 and 12, nor does the Office Action state that it does. Instead, WO '685 merely discloses coating formulations for sustained-release drug implants that include pore forming agents. Accordingly, Applicants request that this rejection be withdrawn and respectfully asserts claims 6 and 18 are also in condition for allowance.

Conclusion

Applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. In view of the foregoing amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested, and it is respectfully asserted that the present application is in condition for allowance.

Any claim amendments which are not specifically discussed in the above remarks are not made for patentability purposes, and it is believed that the claims would satisfy the statutory requirements for patentability without the entry of such amendments. Rather, these amendments have only been made to increase claim readability, to improve grammar, and to reduce the time and effort required of those in the art to clearly understand the scope of the claim language. They are simply additional specific statements of inventive concepts described in the application as originally filed.

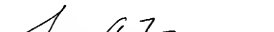
Should the Examiner have any remaining concerns that might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: January 17, 2007

By: 

Gregory A. Hermanson
Registration No. 53,018
Attorney of Record
Customer No. 20,995
(619) 235-8550

3310474
011607